This document is scheduled to be published in the
Federal Register on 01/15/2013 and available online at
http://federalregister.gov/a/2013-00607, and on **FDsys.gov**

4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-N-1248]

Creating an Alternative Approval Pathway for Certain Drugs Intended to Address Unmet Medical Need; Public Hearing; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public hearing; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing a public hearing to obtain input on a potential new pathway to expedite the development of drugs, including biological products, for serious or life-threatening conditions that would address an unmet medical need. The drug's safety and effectiveness would be studied in a smaller subpopulation of patients with more serious manifestations of a condition. Such a pathway could involve smaller and more rapid clinical trials than would occur if the drug were studied in a broader group of patients with a wide range of clinical manifestations. The labeling of drugs approved using this pathway would make clear that the drug is narrowly indicated for use in limited, well-defined subpopulations in which the drug's benefits have been shown to outweigh its risks. The purpose of the public hearing is to obtain information and comments from the public on the need for and feasibility of this pathway and its potential advantages and disadvantages.

DATES: Dates and Time: The public hearing will be held on February 4 and 5, 2013, from 9 a.m. to 4 p.m. The public hearing may be extended or may end early depending on the level of public participation.

Attendance, Presentations, and Comments: Individuals who wish to attend or present at the public hearing must register on or before 5 p.m. EST on January 22, 2013. To register for the public hearing, email your registration information to ExpeditedPathwayPublicMtg@fda.hhs.gov. Section IV of this document provides attendance and registration information. Either electronic or written comments will be accepted after the hearing until March 1, 2013.

ADDRESSES: The public hearing will be held at FDA's White Oak Campus, 10903 New Hampshire Ave., Building 31 Conference Center, the Great Room (rm. 1503), Silver Spring, MD, 20993-0002. Entrance for the public meeting participants (non-FDA employees) is through Building 1 where routine security check procedures will be performed. For parking and security information, please refer to http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm.

Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

Jonas Santiago,

Center for Drug Evaluation and Research,

Food and Drug Administration,

10903 New Hampshire Ave.,

Silver Spring, MD 20993-0002,

301-796-5346,

FAX: 301-847-3529,

email: ExpeditedPathwayPublicMtg@fda.hhs.gov;

or

Stephen Ripley,

Center for Biologics Evaluation and Research (HFM-17),

Food and Drug Administration,

1401 Rockville Pike, suite 200N,

Rockville, MD 20852-1448,

301-827-6210.

SUPPLEMENTARY INFORMATION:

FDA is announcing a public hearing to obtain input on a potential new pathway for approving drugs, including biological products, targeted at serious or life-threatening conditions and intended to address an unmet medical need. The drug's safety and effectiveness would be studied in a smaller subpopulation of patients with more serious manifestations of a condition. Such a pathway could involve smaller and more rapid clinical trials than would occur if the drug were studied in a broader group of patients with a wide range of clinical manifestations. The labeling of drugs approved using this pathway would make clear that the drug is narrowly indicated for use in limited, well-defined subpopulations in which the drug's benefits have been shown to outweigh the risks.

I. Background

In the last two decades, major advances in molecular and cellular biology have greatly expanded our understanding of a broad range of complex disease processes and have led to major advances in the treatment of conditions such as cystic fibrosis, HIV, hepatitis C, and

multiple sclerosis. In some cases, however, the resource-intensive programs needed for approval of drugs to treat a broad condition with a wide range of clinical manifestations require very large study populations and can hinder the ability to make promising new drugs available in a timely manner to subpopulations of patients with important unmet medical needs. FDA recognizes its role in fostering the application of scientific advances to the treatment of disease through drug development, including the use of novel approaches that can facilitate development of treatment for unmet needs.

Traditional drug development programs are designed to evaluate the benefits and risks of treatment with a high degree of precision for the range of manifestations of a disease or condition. Often this will involve studies that expose a large number of patients to the drug, normally for an extended period of time. In some cases, such as when safety issues have arisen with prior drugs in a class, additional trials are needed to help identify serious but infrequent risks. Typically, these studies are needed when there is an expectation that the drug will be used broadly in patients with less severe manifestations of the condition.

Existing processes to expedite drug development and review of important new therapies have worked effectively in many circumstances. For example, more than 100 new therapies and indications have been approved under the accelerated approval process (21 CFR part 314, subpart H; 21 CFR part 601, subpart E).[1] In addition, FDA's existing flexibility in applying the statutory requirements for approval has effectively facilitated development of drugs for conditions where the entire intended patient population has serious unmet medical needs. However, FDA believes that it is important to explore the need for and feasibility of a new

---

[1] See a list of Center for Drug Evaluation and Research Drug and Biologic Accelerated Approvals as of September 30, 2011, available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM278506.pdf.

process focused on developing drugs for subpopulations of patients with serious or life-threatening conditions, including patients with serious or life-threatening infections caused by antibiotic-resistant bacteria.

II. New Pathway

FDA is seeking input on a potential new pathway to approve drugs for use in limited, well-defined subpopulations of patients with serious or life-threatening conditions for whom the benefits of the drug have been shown to outweigh the risks. The pathway could include product labeling with a specific designation to make clear that the drug indication is limited to the narrow subpopulation and the rationale for limiting use to that population. The pathway also might provide for the designation and an appropriate logo to appear on a drug's container label.

This designation could be designed to inform the health care community, including practitioners, payers, and patients, of compelling reasons to carefully manage use of such drugs, limiting use to appropriate patients, as the benefit-risk profile only warrants use in the identified subpopulation. In addition, the potential new pathway could be used to help reduce the development of resistance to important antibacterial drugs by limiting their use to those patients in whom use is appropriate and necessary.

This approval of a narrow indication could be broadened if additional data become available which demonstrate the safety and effectiveness of the drug in treating a broader condition or patient population. For example, a drug could be initially approved using this pathway for a narrow subpopulation of patients because of uncertainty about a cardiovascular risk that would not be acceptable in a broad population. If a long-term study subsequently demonstrates that the benefit-risk profile makes the drug appropriate for broader use, the designation could be removed. Alternatively, there may be drugs for which we would not

anticipate the possibility of approval in the broader population, such as when there is a known toxicity that, while acceptable in patients with serious manifestations of a condition, would not be appropriate for use in patients with milder manifestations of the condition.

The proposed pathway was recommended by the President's Council of Advisors on Science and Technology (PCAST) in their September 2012 "Report to the President on Propelling Innovation in Drug Discovery, Development, and Evaluation," as a way to improve drug evaluation. The PCAST recommendations support the goal of increasing the output of innovative, new medicines for patients with important unmet medical needs, while increasing drug efficacy and safety, through industry, academia, and government working together to decrease clinical failure, clinical trial costs, time to market, and regulatory uncertainty.[2]

III. Scope of the Public Hearing and Discussion Questions

FDA is holding this public hearing to seek input from interested members of the public including patients and consumers, practitioners and other members of the medical community, regulated industry, insurers, and managed care organizations on a potential new pathway to approve drugs shown to be safe and effective in a subpopulation of patients with serious or life-threatening conditions in which an unmet medical need exists. FDA is interested in obtaining information and public comment on the following issues:

1. Considering existing processes to expedite drug development and review of important new therapies (i.e., accelerated approval, fast-track designation), would this new pathway increase the therapeutic options for serious or life-threatening conditions for which an unmet medical need exists? If not, what might be some alternative approaches?

---

[2] For more information on the PCAST Report to the President on Propelling Innovation in Drug Discovery, Development, and Evaluation, see http://www.whitehouse.gov/sites/default/files/microsites/ostp/pcast-fda-final.pdf.

2. Can you identify specific serious or life-threatening conditions for which an unmet medical need exists and for which this approval pathway may benefit subpopulations of patients?

3. What approaches could be undertaken (by FDA or by people or organizations other than FDA) to monitor use of drugs approved under this pathway to determine whether they are being used inconsistent with the terms of approval? What approaches could be undertaken to prevent, manage, or monitor use in a broader population where safety and efficacy has not been demonstrated? For example, if this pathway were adopted to approve new antibacterial drugs when limited use was needed (e.g., to prevent the emergence of further antimicrobial resistance), what other measures (by FDA or by people or organizations other than FDA) might ensure that these products are used appropriately only in the indicated subpopulations?

4. Would this pathway help to address some of the current challenges in antibacterial drug development, particularly for serious or life-threatening infections for which there is an unmet medical need?

5. This potential pathway could be used to approve drugs for a limited subpopulation based upon smaller clinical trials, when benefit-risk is appropriate for the limited population but safety and efficacy have not been demonstrated for use in a broader population of patients or patients with less severe manifestations of the condition. For the serious or life-threatening conditions you identified in question 2, what benefit-risk considerations need to be taken into account before and after marketing and how should they be addressed?

6. Would the use of a formal designation and logo to reflect approval under this pathway, with clear labeling of clinical information that only supports use in the indicated subpopulation, but without other constraints from FDA be effective in limiting use to the indicated subpopulation? Why or why not?

IV. Attendance, Registration, and Requests for Oral Presentations

The public hearing is free and seating will be on a first-come, first-served basis. Attendees, including those not presenting, need to register for the public hearing.

If you wish to attend or make an oral presentation during the hearing, you must register by submitting either an electronic or written request received on or before January 22, 2013. (See FOR FURTHER INFORMATION CONTACT.) You must provide your name, title, business affiliation (if applicable), address, telephone and fax numbers, email address, and type of organization you represent (e.g., industry, consumer organization). If requesting to present, you also should submit a brief summary of the presentation, including the discussion question(s) that will be addressed and the approximate time requested for your presentation. FDA has included discussion questions in section III of this document. You should identify the question(s) and the number of each question you wish to address in your presentation. We encourage individuals and organizations with common interests to consolidate or coordinate their presentations to allow adequate time for each request for presentation. FDA will do its best to accommodate requests to speak and will determine the amount of time allotted for each oral presentation, and the approximate time that each oral presentation is scheduled to begin. Persons registered to make an oral presentation should submit to FDA an electronic copy of their presentation and an abstract to ExpeditedPathwayPublicMtg@fda.hhs.gov on or before January 30, 2013.

If you need special accommodations because of a disability, please contact Jonas Santiago (see FOR FURTHER INFORMATION CONTACT) at least 7 days before the meeting.

V. Notice of Hearing Under 21 CFR Part 15

The Commissioner of Food and Drugs is announcing that the public hearing will be held in accordance with part 15 (21 CFR part 15). The hearing will be conducted by a presiding officer, who will be accompanied by FDA senior management.

Under § 15.30(f), the hearing is informal and the rules of evidence do not apply. No participant may interrupt the presentation of another participant. Only the presiding officer and panel members may question any person during or at the conclusion of each presentation.

Public hearings under part 15 are subject to FDA's policy and procedures for electronic media coverage of FDA's public administrative proceedings (part 10 (21 CFR part 10, subpart C)). Under § 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants. The hearing will be transcribed as stipulated in § 15.30(b) (see section VII of this document).

To the extent that the conditions for the hearing, as described in this notice, conflict with any provisions set out in part 15, this notice acts as a waiver of those provisions as specified in § 15.30(h).

VI. Comments

Interested persons may submit either electronic comments to http://www.regulations.gov or written comments regarding this document to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. In addition, when responding to specific questions as discussed in section III of this document, please identify the question you are addressing. Received comments may be seen in the Division of Dockets Management

between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

VII. Transcripts

Transcripts of the public hearing will be available for review at the Division of Dockets Management (see ADDRESSES) and on the Internet at http://www.regulations.gov approximately 30 days after the public hearing. A transcript will also be made available in either hard copy or on CD-ROM, upon submission of a Freedom of Information request. Written requests are to be sent to the Division of Freedom of Information (ELEM–1029), Food and Drug Administration, 12420 Parklawn Dr., Element Bldg., Rockville, MD 20857.

Dated: January 9, 2013.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2013-00607 Filed 01/14/2013 at 8:45 am; Publication Date: 01/15/2013]